Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of the claims in the application:

Listing of Claims:

1.   (Original) A crystal comprising at least 150 amino acid residues of the LXRβ ligand binding domain.

2.   (Currently Amended) A crystal according to claim 1 comprising the amino acid sequence from Leu-220 to Glu-461 of a human LXRβ shown in <u>Figure 5a (SEQ ID NO: 1)</u> ~~Figure 5~~ or an amino acid sequence having at least 95% identity with the sequence and which encodes for a LXRβ ligand binding domain.

3.   (Previously Presented) A crystal according to claim 1, comprising the entire LXRβ ligand binding domain.

4.   (Previously Presented) A crystal according to claim 1, produced using a sequence including helix 12 of LXRβ.

5.   (Previously Presented) A crystal according to claim 1, usable in X-ray crystallography.

6.   (Previously Presented) A crystal according to claim 1, including a ligand bound to LXRβ or a portion thereof.

7.   (Previously Presented) A crystal according to claim 6 in which the ligand is T0901317, GW3965 or any other ligand that binds with an affinity of $IC_{50} < 1000$ nM to the internal LXRβ binding cavity.

8.   (Original) A crystal of LXRβ LBD belonging to the space group $P2_12_12_1$ and having the unit cell dimensions a = 59 +/-3 Å, b = 100 +/-5 Å, c = 176 +/-3 Å, α = β = γ = 90°.

9.   (Original) A crystal of LXRβ LBD belonging to the space group $P6_122$ and having the unit cell dimensions a=59 +/-3 Å b= 59+/-3 Å c=294 +/-3 Å , α = β = 90°, γ = 120°.

10.   (Original) A crystal of LXRβ LBD in complex with a coactivator peptide (TIF2 NR-box 1) belonging to the space group $P2_12_12$ and having the unit cell dimensions a= 89+/-3, b= 91+/-3, c=131+/-3, α = β = γ = 90°.

11.   (Previously Presented) A crystal according to claim 1, having a resolution determined by X-ray crystallography of better than 3.6 Å.

12.   (Original) A crystal according to claim 11 having a resolution determined by X-ray crystallography of better than 2.9 Å.

13.   (Previously Presented) A drug screening assay comprising the steps of:

(a)   selecting a potential ligand by performing rational drug design with the three-dimensional structure determined for the crystal of claim 1, wherein said selecting is performed in conjunction with computer modelling;

(b)   contacting (i.e. docking) the potential ligand with the ligand binding domain of LXRβ;   and

(c)   detecting the binding of the potential ligand for the ligand binding domain.

14.   (Original) A method according to claim 13, wherein a potential drug is selected on the basis of it having a greater affinity for the ligand domain of LXRβ than that of a standard ligand for the ligand binding domain of LXRβ.

15.   (Original) The method of claim 14 wherein the standard ligand in step (c) is T0901317, GW3965, or 24(S),25-epoxycholesterol.

16.   (Previously Presented) The method of claim 13, further comprising the step of:

(d)   growing a supplemental crystal containing a protein ligand complex formed between the N-terminal truncated LXRβ and the potential drug, wherein the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 5.0 Å;

(e)   determining the three-dimensional structure of the supplemental crystal with molecular replacement analysis;

(f)   selecting a candidate drug by performing a rational drug design with the three-dimensional structure determined for the supplemental crystal, wherein said selecting is performed in conjunction with computer modelling;

(g)   contacting a cell that expresses LXRβ; and

(h)   detecting a measure of protein synthesis in the cell; wherein a candidate drug is identified as such a drug when it inhibits or enhances the expression of protein synthesis in the cell.

17.   (Original) The method of claim 16 further comprising an initial step that precedes steps (a) wherein initial step consists of determining the three-dimensional structure of a crystal comprising a protein-ligand complex formed between an N-terminal truncated LXRβ and T0901317, GW3965, or 24(S),25-epoxycholesterol, wherein the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 5.0 Å.

18.   (Previously Presented) A drug screening assay comprising the steps of:

(a)   selecting a potential ligand by performing rational drug design with the three-dimensional structure determined for the crystal of claim 1, wherein said selecting is performed in conjunction with computer modelling;

(b)   adding the potential ligand to a cDNA or protein expression assay regulated by LXRβ; and

(c)   detecting a measure of a cDNA or protein expression; wherein a potential ligand that regulates the expression of protein expression is selected as a potential drug.

19.   (Original) The method of claim 18 wherein said protein expression is an in vitro protein expression assay.

20.   (Previously Presented) A machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when using a machine programmed with instructions for using said data, is capable of displaying a graphical three-dimensional representation of a crystal structure according to claim 1 or a homologue of said crystal structure.

21.   (Previously Presented) A method for designing a potential LXRβ ligand for the treatment of diseases modulated by the natural LXRβ ligand, the method comprising the steps of:

    (a)   performing a fitting operation between the chemical entity and a binding site of LXRβ receptors identified from a machine-readable storage medium according to claim 20; and

    (b)   analyzing the results of the fitting operation to predict the association between the potential LXRβ ligand and the binding site.

22.   (Original) Method according to claim 21, additionally providing the steps of:

    (c)   synthesizing the potential LXRβ ligand based on the crystal structure of the said receptor; and

    (d)   assaying the LXRβ ligand binding response in a LXRβ animal model cell line by measuring one or more in vivo effects including but not limited to changes in lipoprotein profile, changes in serum or tissue triglyceride levels, changes in serum or tissue cholesterol levels, changes in serum glucose levels,

changes in atherosclerotic lesion size indicating that the LXRβ ligand may be used for treatment of diseases modulated by LXRβ.

23. (Original) A method according to claim 21, additionally providing the steps of:

(e) synthesising the potential LXRβ ligand based on the crystal structure of said receptor; and

(f) assaying the LXRβ ligand binding response in a LXRβ reporter cell line by measuring one or more in vitro effects, including but not limited to changes in the activity of a LXR response element driven reporter gene such as alkaline phosphatase, green fluorescent protein, or luciferase, changes indicating that the LXRβ ligand may be used for treatment of diseases modulated by LXRβ.

24. (Previously Presented) A method according to claim 21, additionally comprising the steps of modifying the potential LXRβ ligand so that it:

(a) sterically displaces helix-12; or

(b) disrupts the dimerisation surface.

25. (Previously Presented) A method according to claim 21, wherein said a potential LXRβ ligand is a LXRβ antagonist.

26. (Previously Presented) A method according to claim 21, wherein said potential LXRβ ligand is an agonist.

27. (Previously Presented) A method according to claim 21, wherein said potential LXRβ ligand is a selective modulator.

28. (Currently Amended) A method of designing a ligand which will bind to LXRβ comprising comparing the shape of a compound with the shape of the ligand-binding cavity of LXRβ as obtained from a crystal according to claim 1 ~~claim 1~~, and determining which amino acid or amino acids of the ligand binding domain interact with said compound.

29. (Original) A crystallized molecule or molecular complex comprising a binding pocket defined by the structure coordinates of human LXRβ ligand binding domain amino acid residues Ser242, Phe268, Phe271, Thr272, Leu274, Ala275, Ser278, Ile309, Met312, Leu313, Glu315, Thr316, Arg319, Ile327, Phe329, Leu330, Tyr335, Phe340, Leu345, Phe349, Ile350, Ile353, Phe354, His435, Gln438, Val439, Leu442, Leu449, Leu453, Trp457, according to the co-ordinate tables or a homologue of said molecule or molecular complex wherein said homologue has a root mean square deviation form the backbone atoms of said amino acids of not more than 1.5Å.

30. (Original) A crystallisable composition comprising at least 150 amino acid residues of the LXRβ ligand-binding domain.

31. (Currently Amended) An isolated protein consisting essentially of the amino acid sequence shown from amino acid 220 to amino acid 461 in Figure 5a (SEQ ID NO: 1) or the sequence shown in Figure 5b (SEQ ID NO: 2).

32. (Original) An isolated protein according to claim 31, additionally comprising a tag, such as a his-tag.

33. (Currently Amended) A vector, such as a plasmid, containing a nucleic acid molecule encoding a protein consisting of the amino acid sequence shown from 220 to 461 in <u>Figure 5a (SEQ ID NO: 1)</u> ~~Figure 5~~ or the sequence shown in Figure 5b <u>(SEQ ID NO: 2)</u>.

34. (Original) A host cell containing a vector according to claim 33.

35. (Previously Presented)   An isolated protein having an amino acid sequence identical to the amino acid sequence used in a crystal according to claim 1.

36. (Original) A computer for producing a three-dimensional representation of:

(a)   a molecule or molecular complex, wherein said molecule or molecular complex comprises a binding pocket defined by the structure coordinates of LXRβ amino acid residues Ser242, Phe268, Phe271, Thr272, Leu274, Ala275, Ser278, Ile309, Met312, Leu313, Glu315, Thr316, Arg319, Ile327, Phe329, Leu330, Tyr335, Phe340, Leu345, Phe349, Ile350, Ile353, Phe354, His435, Gln438, Val439, Leu442, Leu449, Leu453, Trp457 according to the co-ordinate tables; or

(b)   a homolog of said molecule or molecular complex, wherein said homolog comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Å, wherein said computer comprises:

(i)   a computer-readable data storage medium comprising a data storagematerial encoded with computer-readable data, wherein said data comprises the structure of LXRβ amino acid residues Ser242, Phe268, Phe271, Thr272,

Leu274, Ala275, Ser278, Ile309, Met312, Leu313, Glu315, Thr316, Arg319, Ile327, Phe329, Leu330, Tyr335, Phe340, Leu345, Phe349, Ile350, Ile353, Phe354, His435, Gln438, Val439, Leu442, Leu449, Leu453, Trp457 according to the co-ordinate tables;

(ii) a working memory of storing instructions for processing said computer-readable data;

(iii)   a central-processing unit coupled to said working memory and to said computer-readable data storage medium for processing and computer-machine readable data into said three-dimensional representation; and

(iv) a display coupled to said central-processing unit for displaying said three-dimensional representation.

37. (Original) The computer according to claim 36 wherein said computer produces a three-dimensional representation of:

(a)   a molecule or molecular complex defined by structure coordinates of all of the LXRβ ligand binding domain amino acid residues set forth in the co-ordinate tables; or

(b)   a homolog of said molecule or molecular complex, wherein said homolog comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Å; and wherein said computer readable data contains the coordinates of all of the LXRβ ligand binding domain amino acid residues as set forth in the co-ordinate tables.

38. (Currently Amended) A method for determining the three-dimensional structure of a complex between LXRβ and a ligand therefore, which comprises:

(a)   obtaining x-ray diffraction data for crystals of the complex as defined in claim 1 ~~claim 1~~; and

(b)   utilizing a set of atomic coordinates as defined in claim 29 or a portion thereof; and coordinates having a root mean square deviation therefrom with respect to conserved protein backbone atoms of not more than 1.5Å to define the three-dimensional structure of the complex.

39.   (Original) A method for determining a modelling structure of a protein containing LXRβ or a complex of said protein and a ligand, which method comprises:

(a)   providing a three-dimensional structure defined by a set of coordinates as defined in claim 29, or a portion thereof; and coordinates having a root mean square deviation therefrom with respect to conserved protein backbone atoms of not more than 1.5Å;

(b)   generating a three-dimensional model structure of the protein containing LXRβ using a homology modelling method and the structure of step (a) as a template; and

(c)   subjecting the resulting model to molecular mechanics energy minimization.